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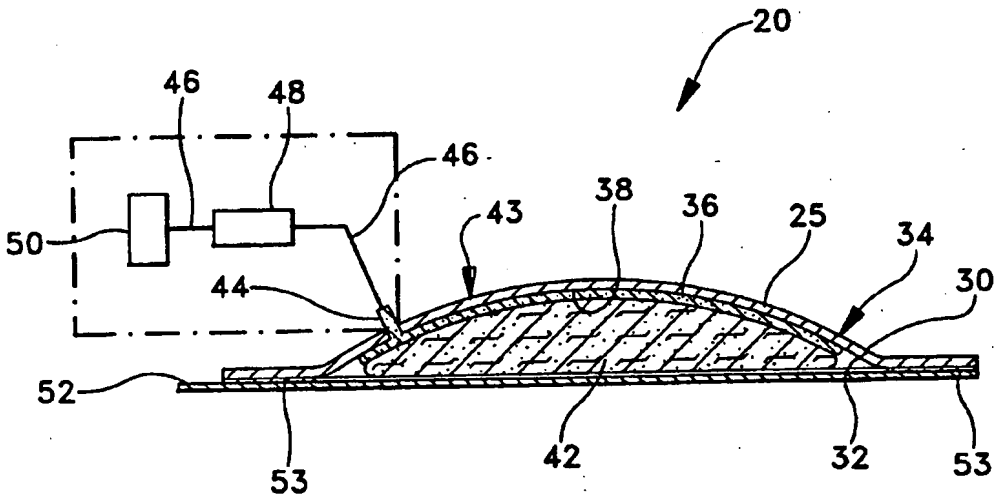

(57) Abstract

An iontophoretic drug delivery device (20) with a flexible active electrode assembly (25) may include at least one flexible active electrode, at least one reservoir (42) and a container or holder (43) for holding the reservoir and electrode in electrical communication. The flexible active electrode device includes an active metal electrode (36) on a flexible backing (30). The active metal electrode is bonded to a portion of the backing in a pre-selected pattern (40) leaving a portion (41) of the surface (32) of the flexible backing exposed. The flexible active metal electrode contains a metal selected from the group including silver, copper and molybdenum and may contain an insoluble halogen salt of the metal. The electrode may be formed from at least one electro-conductive ink applied in a pre-selected pattern to the flexible backing or alternatively may be formed by application of a layer of metallic silver to a conductive first metal layer electrode circuit or an inert conductive ink electrode circuit which is bonded to the flexible backing.

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ACTIVE DRUG DELIVERY DEVICE, ELECTRODE, AND METHOD FOR MAKING SAME

FIELD OF THE INVENTION

The present invention generally relates to active devices for delivering a medicament to a patient transdermally, i.e., through the skin, and more specifically relates to an active flexible electrode which can be used in an iontophoretic device and a method for making same.

BACKGROUND OF THE INVENTION

Transdermal administration provides a method by which a medicament can be delivered in a controlled manner to target tissues either for localized effect or for systemic absorption. The transdermal administration of a medicament offers the advantage of being a noninvasive procedure which does not require percutaneous puncture devices, and further, avoids placing stability requirements on the medicament if it is to be introduced through the gastrointestinal tract. Additionally, transdermal administration is ideally suited for sustained delivery of a medicament instead of the bolus dosage characteristic of most other modes.

There are two general types of transdermal drug delivery techniques i.e., "Passive" and "Active".

The passive technique is traceable to biblical times when healing oils and medicaments were applied to the skin of a patient. Passive transdermal drug delivery has its basis in natural physical phenomena such as osmosis, diffusion and differential solubility.

Active transdermal delivery was first reported in 1908 when it was demonstrated that ions could be driven across the skin by means of an electric current. The active techniques are termed iontophoresis, electro-osmosis and electrophoresis and are collectively referred to here simply as iontophoresis.

Presently, passive transdermal systems are most effective and used in the delivery of unionized lipophilic moieties which are active at low concentrations, e.g., nitroglycerin, nicotine, estrogen and others. Iontophoresis enables ionized solutes to be delivered transdermally and further allows control of delivery rate and duration of delivery.

Conventional iontophoretic devices, such as those described in U.S. Patent Nos. 4,820,263 (Spevak et al.), 4,927,408 (Haak et al.), and 5,084,006 (Lew et al.), the disclosures of which are hereby incorporated by reference, are for actively delivering a medicament transdermally. Basically, these devices consist of two electrodes, i.e., a cathode and an anode. Both of these electrodes are disposed so as to be in electrical contact with some

portion of the skin or other area of the patient, such as a mucous membrane. One electrode called the donor electrode, is the electrode from which the ionic substance, medicament, drug precursor or drug is delivered into the body by iontophoresis. The other electrode, called the counter or return electrode, serves to close the electrical circuit through the body. In conjunction with the patient's skin contacted by the electrodes, the circuit is completed by connection of the electrodes to a source of electrical energy, e.g., a battery. In the case where the ionic substance to be delivered into the body is positively charged, i.e., a cation, then the anode will be the donor electrode and the cathode will serve to complete the circuit. If the ionic substance to be delivered is negatively charged, i.e., an anion, then the cathode will be the donor electrode and the anode will be the counter electrode. Further, it may be possible to deliver two drugs simultaneously by providing a cationic drug at the anode and an anionic drug at the cathode.

Iontophoresis should be suitable for noninvasively delivering a medicament over a sustained period. It is often desirable to maintain a certain constant level of medicaments in the patient's system instead of periodically injecting a bolus dosage. In many current iontophoretic systems, such sustained delivery is not practical because of the danger of electrical and chemical burns. U. S. Patent 4,752,285 (Petelenz et al.), the disclosure of which is herein incorporated by

reference, teaches these burns may stem from two sources, galvanic where the electrical current itself causes burns, and chemical where extremes in pH (which develop during the iontophoretic process) act in conjunction with electric current to cause chemical burns.

Galvanic burns can be minimized or reduced by keeping the current density per unit area of skin below threshold values at which burning begins. Low current densities can be achieved by attention to design so as to maintain uniform electrode contact with the skin. Avoidance of folds, wrinkles and partial contact of the device electrode surface with the patient's skin, all help to eliminate high current density which induces galvanic burns.

U. S. Patent No. 4,883,457 (Sibalis), the disclosure of which is herein incorporated by reference, teaches a multi-layer electrophoretic or electro-osmotic dispensing device with multiple reservoirs using conductors from electroconductive graphite paint. There is no suggestion that these conductors be active electrodes. The multiple layers can be fabricated by a multi-step silk screen printing or transfer process.

In addition, it has been suggested by the art that multiple electrodes and highly flexible devices may be useful in ensuring uniform contact with the patient's skin to avoid galvanic burns. Highly flexible devices are less likely to partially lift off the area of the patient's skin where they are

placed, thus avoiding spots of high current density. The use of multiple small electrodes each with its own reservoir allow each electrode area to be maintained in uniform contact with the placement area on the patient's skin.

While galvanic burns may be substantially controlled by the device design, the control of pH and the resulting burns caused by extremes in the alkalinity or acidity of the medicament solution during passage of electric current requires an understanding of the electron transfer processes which occur during active transdermal delivery. As the current passes between the electrode and the medium containing medicament, at a voltage greater than 1.23 relative to the standard hydrogen electrode (SHE) at the positive pole, the voltage necessary for electrolysis of water, there is increased production of hydrogen ions (H^+) or at the negative pole, 0.83 volts (SHE) for the production of hydroxide ions (OH^-). When the iontophoresis electrode is nonreactive, an increase in H^+ and OH^- ion concentration is caused by the exchange of charge through the electrolysis of water.

Since the H^+ and OH^- ions which result from the electrolysis of water are extremely mobile, they migrate rapidly through the electrolyte solution away from the electrode and toward the skin of the patient. Thus, an area of extreme pH is ultimately created directly adjacent to the skin. This area of extreme pH is clearly undesirable and serious burns have been observed when these ions are actively transported through the skin.

The problem of electrolysis of water with its concomitant generation of H^+ and OH^- ions can be addressed by keeping the electrode potential below 1.23 volts relative to (SHE), or by the use of an electrode which is capable of reacting with the complementary ion of the medicament to form an insoluble precipitate at a voltage potential below the voltage potential for the electrolysis of water. The incorporation of a reactive electrode system into an iontophoretic device substantially eliminates the generation of H^+ and OH^- ions, thus avoiding attack of the skin while maintaining the medicament at a desired pH. The use of an active electrode system with a counter ion which forms a precipitate with the electrode ion further precludes competition for transport between the counter ion and the medicament. A electrode formed from silver in conjunction with a chloride counter ion for the medicament fulfills the requirements for a reactive electrode system. While silver has been shown to perform satisfactorily in an iontophoretic system, cost constrains its use in commercial devices.

The problem of burning a patient's skin during iontophoresis thus can be substantially reduced by ensuring intimate and uniform contact between an iontophoretic delivery device and the skin and incorporation of a reactive electrode into the device.

As described above, fulfillment of the requirement for intimate and uniform contact is

facilitated by highly flexible devices and multiple electrodes. Nowhere in the art has there been a recognition that these design features could be coupled with a reactive electrode such as silver, copper or molybdenum thereby providing a significant improvement in the art of iontophoresis. Further, there has also been a need for a way to couple these design features with the ability to readily manufacture the device, while providing flexibility and minimizing the amount of silver used to improve the feasibility of widespread use of iontophoresis, thereby enhancing benefits to patients. Such methods and apparatus are disclosed and claimed herein.

SUMMARY OF THE INVENTION

In contrast to the prior devices discussed above, it has been found that an iontophoretic device particularly suitable for providing uniform contact with the skin, substantially eliminating burning of patient's skin while improving delivery efficiency by greatly reducing competitive ion transport can be constituted in accordance with the present invention.

The invention includes an iontophoretic delivery device for delivering at least one medicament to an applied area of a patient. The device includes an electrode assembly for driving a medicament for absorption into the applied area to be absorbed by a patient's body. The electrode

assembly includes a flexible backing member. The backing member has an inside surface and an outside surface. The inside surface has a first area which has at least one flexible active electrode of a preselected pattern bonded to it, while a second area of the inside surface of the flexible backing member remains exposed.

The iontophoretic delivery device further includes at least one reservoir for containing the medicament to be delivered situated in electrically conductive relation to the flexible electrode assembly. The device has a holder for holding the electrode assembly. The holder also maintains electrical communication between the electrode assembly and the reservoir.

A flexible active electrode assembly for an active drug delivery device of the present invention includes a flexible backing member with an inside surface and an outside surface. The flexible backing member has an active metal member with a preselected pattern bonded to a first area of the backing member leaving a second area of the backing member exposed. The invention further includes a method for making a flexible active electrode for an active drug delivery device. The method includes providing a flexible backing member with an inside surface and an outside surface. The inside surface has two areas, a first area and a second area. An electroconductive material is applied in a preselected pattern to the first area of the inside surface while leaving the second area of the inside

surface of the backing member exposed.

The flexible active electrode assembly may be formed from at least one electrically conductive ink applied to the backing member or alternatively from a multi-layer active electrode including a layer of silver applied to an inert ink circuit rendered conductive by the inclusion of graphite or an intermediate metal conductive circuit layer bonded to the surface of the backing member. Alternatively, the electroconductive ink may form the active electrode directly by including a first ink containing a metal selected from the group including silver, copper and molybdenum and a second electroconductive ink containing an insoluble halide salt of the metal. Alternatively, an active electrode can be formed from an ink rendered conductive by inclusion of graphite which incorporates a metal selected from the group including silver, copper and molybdenum. The active electrode may further include an insoluble halide salt of the metal selected.

Alternative embodiments may include a plurality of reservoirs, with a plurality of active electrodes. The active electrode assembly may include a system for activating the plurality of electrodes independently.

An alternative method of assembly may include the backing member as a portion of a continuous web, with a plurality of individual electrodes being formed onto the web, a cutting step may be used to

release the individual electrodes from the web for subsequent assembly into devices. A plurality of iontophoretic devices may be formed on the web by adding reservoirs and holders to a plurality of the flexible active electrode assemblies formed on portions of the continuous web, a cutting step then being used to release the devices from the web.

BRIEF DESCRIPTION OF THE DRAWINGS

The various features, objects, benefits, and advantages of the present invention will become more apparent upon reading the following detailed description of the preferred embodiments along with the appended claims in conjunction with the drawings, wherein like reference numerals identify corresponding components, and:

Fig. 1 is a cross-sectional view of a preferred embodiment of an iontophoretic device of the present invention having a flexible active electrode;

Fig. 2 is a top plan view of the flexible electrode of the present invention;

Figs. 3A-3E are a sequence of perspective views of stages in a preferred method for manufacture of a flexible electrode of the present invention;

Figs. 4A and 4B are enlarged fragmentary, cross-sectional views of a flexible electrode of preferred embodiments of the present invention having a plurality of active metal members wherein the members are formed as (4A) a layered structure and (4B) as an electrically conductive ink;

Fig. 4C is a top plan view of a flexible electrode of the present invention having a plurality of electrodes and electrode circuits; and

Fig. 5 is a top plan view of a plurality of the flexible electrodes of the present invention formed with a flexible backing member as a continuous web.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The active drug delivery device of the present invention is illustrated in Figs. 1-5 and is generally designated as 20. Referring to Figs. 1 and 2, the active drug delivery device of the present invention, preferably an iontophoretic device 20, includes a flexible active electrode assembly 25 and at least one reservoir 42 for containing a medicament.

The electrode assembly 25 includes a flexible backing member 30 with an inside surface 32 and an outside surface 34. The electrode assembly further includes an active metal member 36 bonded to a first area 38 of inside surface 32 in a preselected pattern 40 leaving a second area 41 of surface 32 exposed.

Reservoir 42 is held in electrically conductive relation to the electrode assembly by a container or holder 43 which also serves to hold the flexible electrode assembly and maintain the electrode assembly and reservoir in electrical communication. The holder may include a connector 44 and conductors

46. Device 20 may further include a driver assembly 48 and a counter electrode 50 connected by conductors 46 to complete the electrical circuit.

Device 20 may further include a protective release covering 52 held to the device by a layer of adhesive 53. The layer of adhesive 53 may also serve for mounting the device to an area of a patient to which the medicament is to be applied.

The preferred device 20 may have flexible backing member 30 serve as the backing member for the reservoir, with inside surface 32 also serving as the inside surface of reservoir 42 and outside surface 34 serving as part of holder 43 for the device.

Materials suitable for use as flexible backing member 30 include, but are not limited to, flexible films formed from polyethylene, polyethylene terephthalate, polyvinyl chloride and polyvinylidene fluoride. The particular material is not essential to the present invention as long as it provides flexibility, sufficient support for the active metal member and is compatible with the medicament system.

The method of making the electrode assembly of the present invention is generally shown in Figs. 3A through 3E. The active electrode assembly 25 may be prepared with active metal member 36 bonded to inside surface 32 of flexible backing member 30. A flexible conductive metal layer, preferrably a

flexible foil, 60 forms an electrode circuit 61 which then has a layer of metallic silver 62 bonded thereto to form the active metal member 36, with conductive foil 60 thereby intermediate silver layer 62 and backing member 36. An alternative for formation of active metal member 36 would be to form electrode circuit 61 from an ink rendered conductive by the incorporation of graphite and the like, then bonding metallic silver as a layer thereto.

In a preferred embodiment of this method, as shown in Figs. 3A and 3B, forming the preferred active metal electrode assembly includes bonding a layer of conductive metallic foil 60, preferrably a layer of copper, to inside surface 32 of flexible backing member 30. Preselected pattern 40, a photoresist or the like, as shown in Fig. 3C, is then formed on a surface 63 of foil 60. One skilled in the art will appreciate that the preselected pattern may be simple, as shown in Fig. 2, or complex, with multiple segments and the like. A portion of foil 60 is removed by, for example, etching the surface, with a portion 64 of the preferred foil not included in pattern 40 being removed, thereby forming electrode circuit 61 and exposing second area 41 of surface 32 (Fig. 3D). The etch process may be an acidic dissolution process, an electrochemical enhanced milling process, an ion milling, a laser milling process and the like for removal of portion 64 of the foil to leave electrode circuit 61 as shown in Fig. 3D. The particular process is not material to the present invention and is merely a matter of choice.

In a preferred embodiment, metallic silver layer 62 is then bonded to at least a portion of the electrode circuit 61 forming an active metal member 36, as shown in Fig. 3E. Metallic silver layer 62 may be applied by an electroplating process, vacuum sputtering or any other method which results in a uniform layer of metallic silver being formed over the metallic foil electrode circuit. The preferred embodiment of the instant invention of forming a layer of metallic silver over the metallic foil electrode circuit instead of simply using silver for the entire electrode circuit serves to minimize the amount of the more expensive silver while maximizing the surface contact area of the silver with the reservoir, thereby enhancing the transfer of silver ions to the counter ion. In addition, by applying the silver after etching the foil to form the electrode circuit, waste of the silver is also further eliminated. In addition, it should be appreciated that the amount of silver applied can vary depending upon the intended application. For example, a thicker layer of silver may be applied when the device is to be used for an extended period of time for delivery of larger quantities of medicament. Further, areas of an electrode circuit external to the reservoir may be left free of silver by masking during the silver application. The metallic silver portion may be treated to form silver chloride on its surface. A preferred method of treatment to form the silver chloride would be to treat the silver layer with aqueous hydrochloric acid while applying an electric current to the electrode.

The preferred embodiment shown in Fig. 2 may have active metal member 36 formed from an electrically conductive ink containing a metal selected from the group including silver, copper and molybdenum, all of which form insoluble halide salts, with silver being preferred. The active metal member 36 may be formed from at least one electrically conductive ink applied in preselected pattern 40 on inside surface 32 (Figs. 3A and 3D). The electroconductive ink may further include graphite and an insoluble halide salt of the selected metal. In addition, to provide a counter electrode, a second electroconductive ink containing an insoluble halogen salt of the metal may be applied in a preselected pattern. A more preferred embodiment of the ink includes metallic silver with silver chloride. The techniques for application of ink 54 may include, but are not limited to, impression, lithography, offset, gravure, jet application, silkscreen and the like. One skilled in the art of application of electroconductive inks will recognize that the electroconductive inks containing one of the metals selected from the group silver, copper and molybdenum with or without the insoluble halide salt of the selected metal may be applied so as to maximize the surface exposure of the included metal and halide, thereby ensuring maximum utilization of the metal and function of the electrode. The aforementioned ink application techniques may easily be utilized to apply preselected patterns of more than one electro-conductive ink for more than one circuit to a device, analogous to multicolor printing processes.

The active electrode embodiment with a silver anode is preferred for cationic drugs having a chloride anion because silver chloride is very insoluble in aqueous systems and further, many cationic drugs are readily available and stable as the hydrochloride salts. An iontophoretic delivery of such a drug with a silver anode, i.e., an active silver electrode, will result in the oxidation of silver to silver ion at the anode surface. The silver ion will react with the available chloride ion from the reservoir and precipitate near the electrode. Consequently, the drug cation will migrate from the reservoir into the patient with greater efficiency than in the case where the drug cation had to compete with the silver cation. This reaction of silver ion with chloride ion is enhanced when silver chloride is incorporated into the electrode as described above. Further because production of H^+ ion is substantially eliminated, pH changes are minimized in the reservoir.

Figs. 4A and 4B show enlarged cross sections of the preferred embodiments of active metal member 36 bonded to inside surface 32 of flexible backing member 30 in preselected pattern 40 leaving second portion 41 of inside surface 32 exposed. Fig. 4A shows the layered embodiment of active metal member 36, i.e. where the active metal, preferably silver, is layered over the electrode circuit formed from a bonded metal layer or from inert electroconductive ink as is shown in Fig. 3D. Fig. 4B shows the embodiment wherein the active metal member is

electroconductive ink which directly incorporates the active metal and/or the insoluble chloride salt of the metal.

As shown in Fig. 4C, any of the preferred embodiments of active metal member 36 may be used to provide a plurality of flexible electrodes 36 which may be formed on a single flexible backing member 30. The plurality of electrodes 36 may be attached to either a first conductor 66 or a second conductor 68. This arrangement of electrodes on two conductors allows the groups of electrodes to be activated independently or simultaneously. This concept may be expanded to a plurality of conductors coupled with a plurality of electrodes to allow electrodes to be activated independently or together by the electrode assembly driver. Alternatively, this ability to form independent electrodes separately in a preselected pattern allows for the formation of a first active electrode circuit containing a metal selected from the group including silver, copper and molybdenum and a second active electrode circuit containing an insoluble halide salt of the metal. The first electrode may include both the active metal and an insoluble halide salt of the active metal. In addition, by allowing for a plurality of electrodes on flexible backing member 30, the instant invention allows more than one medicament to be contained in a plurality of reservoirs associated with the plurality of electrodes. The ability to replicate the electrodes allows a design for the device to provide optimum flexibility to conform to the application site on

the patient thereby minimizing galvanic type burns caused by partial contact, creases and folds.

As shown in Fig. 5, the simple and easily repeated construction of the flexible electrode of the instant invention lends itself to an assembly line process. For example, flexible backing member 30 may be a continuous web 31 and a plurality of flexible electrode assemblies 25 may be applied to the web. Each device may be formed on a portion of the web, to be further assembled into iontophoretic devices. The finished devices could then be released from the web in a final cutting step. An alternative to the completion of an iontophoretic device on the web would be completion of a plurality of flexible electrode assemblies, each on a portion of the web. The individual electrodes would be released from the web by a cutting step followed by subsequent assembly steps to form completed devices.

Thus, while preferred embodiments of the present invention have been described so as to enable one skilled in the art to practice the device, electrode and method of the present invention, it is to be understood that variations and modifications may be employed without departing from the concept and intent of the present invention as defined in the following claims. Accordingly, the preceding description is intended to be exemplary and should not be used to limit the scope of the invention. The scope of the invention should be determined only by reference to the following claims.

What is claimed is:

1. A flexible electrode assembly for an active drug delivery device, comprising:

a flexible backing member having an inside surface and an outside surface; and

an active metal member having a preselected pattern formed on a first area of said inside surface of said flexible backing member with a second area of said inside surface of said flexible member being exposed.

2. The electrode assembly of claim 1 wherein said active metal member includes at least one electrically conductive ink, said electrically conductive ink forming a preselected application pattern on said flexible backing member.

3. The electrode assembly of claim 2 wherein said electroconductive ink contains a metal selected from the group consisting of silver, copper and molybdenum.

4. The electrode assembly of claim 2 wherein a first of said electroconductive inks contains a metal selected from the group consisting of silver, copper and molybdenum, and a second of said electroconductive inks contains an insoluble halogen salt of said metal.

5. The electrode assembly of claim 2 wherein at least one of said inks includes a metal selected from the group consisting of silver, copper and

molybdenum, and an insoluble halide salt of said metal.

6. The electrode assembly of claim 5 wherein at least one of said inks includes silver, graphite and silver chloride.

7. The electrode assembly of claim 1 wherein said active metal member further comprises:

a first layer of electrically conductive metal bonded to said first area of said inside surface of said flexible backing member in a preselected pattern to form an electrode circuit; and

a layer of metallic silver bonded to at least a portion of said conductive first metal layer, with said conductive first metal layer being intermediate said flexible backing member and said metallic silver layer.

8. The electrode assembly of claim 1 wherein said active metal member further comprises:

an electroconductive ink applied to said first area of said inside surface of said flexible backing in a preselected pattern to form an electrode circuit; and

a layer of metallic silver bonded to at least a portion of said electroconductive ink, said conductive ink layer being intermediate said flexible backing member and said metallic silver layer.

9. The electrode assembly of claim 8 wherein said electroconductive ink includes graphite as a conductive component.

10. The electrode assembly of claim 8 wherein said metallic silver has an external surface, said surface being treated to form a layer of silver chloride thereon.

11. The electrode assembly of claim 1 wherein said flexible backing member includes a portion of a continuous web.

12. A method for forming a flexible electrode assembly for an active drug delivery device comprising the steps of:

providing a flexible backing member having an inside surface and an outside surface, said inside surface having a first area and a second area;

applying at least one electroconductive material to said first area of said inside surface of said flexible backing member in a preselected pattern, with said second area of said flexible backing member being exposed.

13. The method of claim 12 wherein the step of applying said electroconductive material includes a metal selected from the group consisting of silver, copper and molybdenum.

14. The method of claim 12 wherein the step of applying said electroconductive material further comprises applying at least one electroconductive ink.

15. The method of claim 14 wherein the step of applying said electroconductive ink includes

applying a first ink containing a metal selected from the group consisting of silver, copper and molybdenum.

16. The method of claim 15 further including applying said first ink containing a metal selected from the group consisting of silver, copper and molybdenum to a first portion of said first area of said backing member and applying a second electro-conductive ink containing an insoluble halogen salt of said metal to a second portion of said first area of said backing member.

17. The method of claim 14 wherein the step of applying said electroconductive ink includes an ink containing graphite, silver and silver chloride.

18. The method of claim 14 wherein the step of applying an electroconductive ink includes a method selected from the group consisting of impression, lithography, offset, gravure, jet application, and silkscreening.

19. The method of claim 12 wherein the step of applying said electroconductive material further comprises the steps of:

bonding a first layer of said electrically conductive metal to said first area and said second area of said inside surface of said flexible backing member;

forming a preselected photoresist pattern onto said first metal layer, said pattern including a first portion of said first metal layer substantial-

ly corresponding to said first area of said flexible backing member;

etching said first metal layer to expose said second area of said flexible member to form a flexible electrode circuit from said first portion of said first metal layer; and

applying a layer of said metallic silver to at least a portion of said electrode circuit, with said first metal layer being intermediate said layer of said metallic silver and said flexible backing member.

20. A device for actively delivering at least one medicament to an applied area of a patient, through, for example, iontophoresis comprising:

electrode assembly means for driving a medicament into the applied area of the patient to be absorbed by the body of the patient, said electrode assembly means including a flexible backing member having an inside surface and an outside surface, said inside surface having a first area and a second area, said electrode assembly means further including at least one flexible active electrode having a preselected pattern bonded to said first area of said inside surface of said flexible backing member with second area of said inside surface of said flexible backing member being exposed;

at least one reservoir for containing a medicament situated in electrically conductive relation to said flexible electrode assembly means; and

holding means for holding said electrode

assembly means and said reservoir and for maintaining said flexible electrode assembly means in electrical communication with said reservoir.

21. The device of claim 20 wherein at least one of said active electrodes contains a metal selected from the group consisting of silver, copper and molybdenum.

22. The device of claim 20 wherein said active electrode assembly comprises a preselected pattern of at least one electroconductive ink applied to said first area of said inside surface of said flexible backing member.

23. The device of claim 22 wherein a first of said electroconductive inks contains a metal selected from the group consisting of silver, copper and molybdenum.

24. The device of claim 22 wherein a first of said electroconductive inks includes graphite, a metal selected from the group consisting of silver, copper and molybdenum and an insoluble halide salt of said metal.

25. The device of claim 22 wherein said first electroconductive ink contains a metal selected from the group consisting of silver, copper and molybdenum being applied to a first portion of said first area of said flexible backing and a second electroconductive ink containing an insoluble halogen salt of said metal being applied to a second

portion of said first area of said flexible backing.

26. The device of claim 22 wherein said electroconductive inks are applied by a technique selected from the group consisting of impression, lithography, offset, gravure, jet application and silkscreen.

27. The device of claim 20 wherein said active metal electrode comprises:

an electrically conductive first metal layer formed in a preselected pattern and bonded to said first area of said inside surface of said flexible backing material to form an electrode circuit; and

a layer of metallic silver bonded to at least a portion of said electrode circuit with said conductive first metal layer thereby being intermediate said flexible backing member and said metallic silver layer.

28. The device of claim 20 wherein said flexible backing member being a backing portion for said reservoir with said inside surface of said flexible backing member being adjacent an inside surface of said reservoir with said outside surface of said flexible backing member being adjacent an outside surface of said reservoir.

29. The device of claim 20 wherein said device includes a plurality of reservoirs and said flexible electrode assembly means includes a plurality of said active electrodes.

30. The device of claim 29 wherein said flexible electrode assembly means includes means for activating said plurality of electrodes independently of one another.

31. The device of claim 20 wherein said flexible backing member includes a portion of a continuous web.

FIG-1

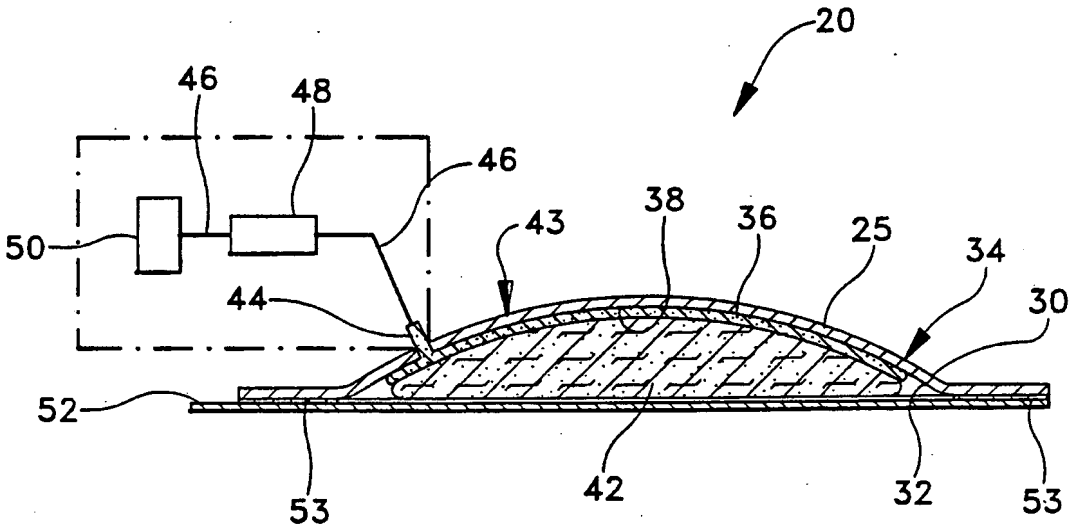


FIG-2

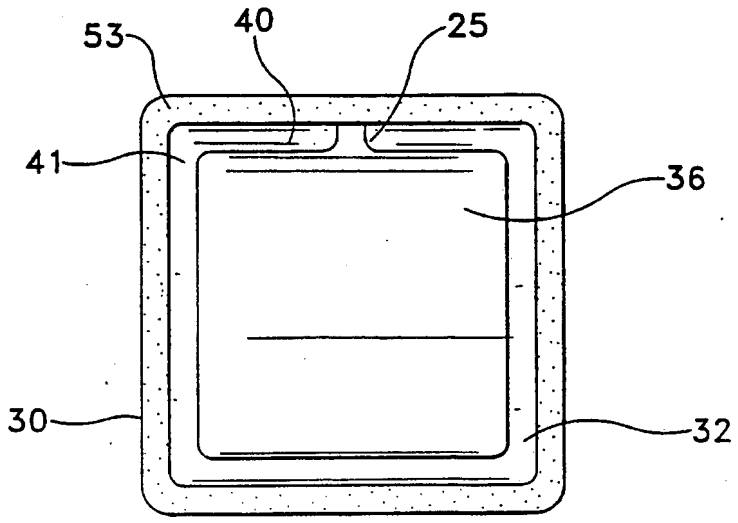


FIG-3A

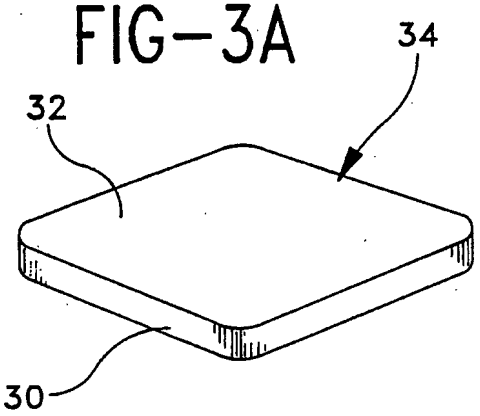


FIG-3B

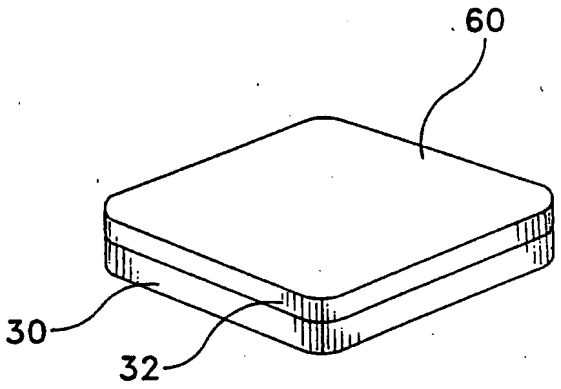


FIG-3C

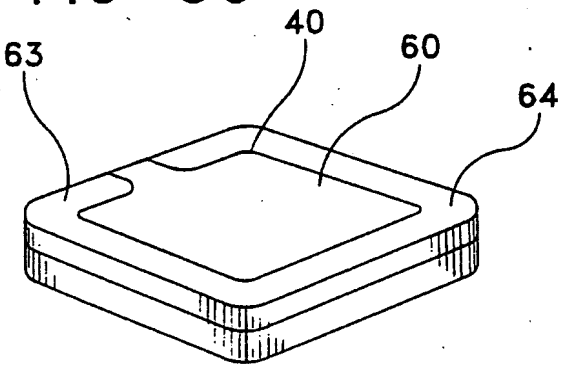


FIG-3D

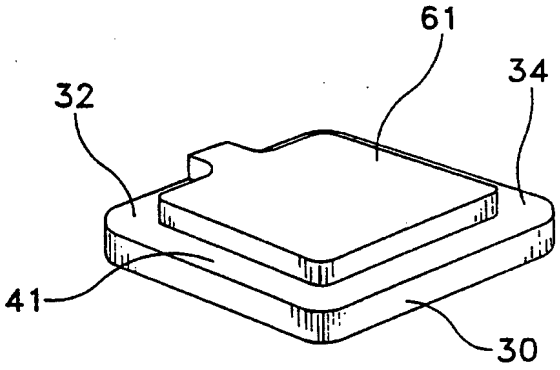


FIG-3E

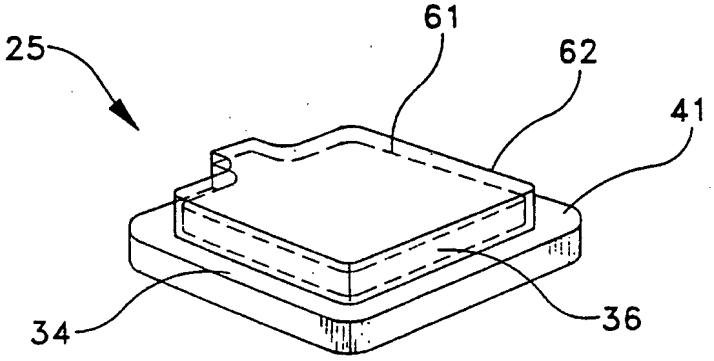


FIG-4A

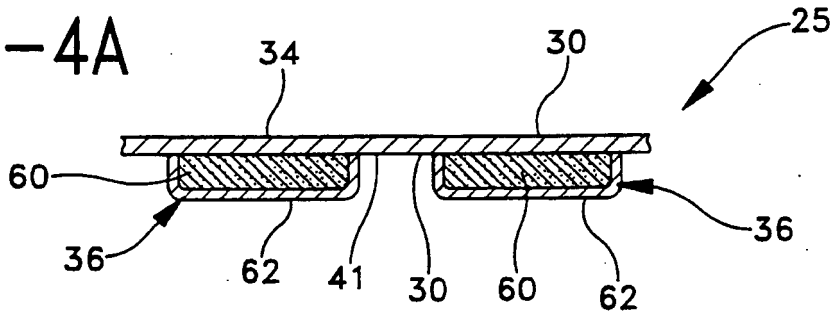


FIG-4B

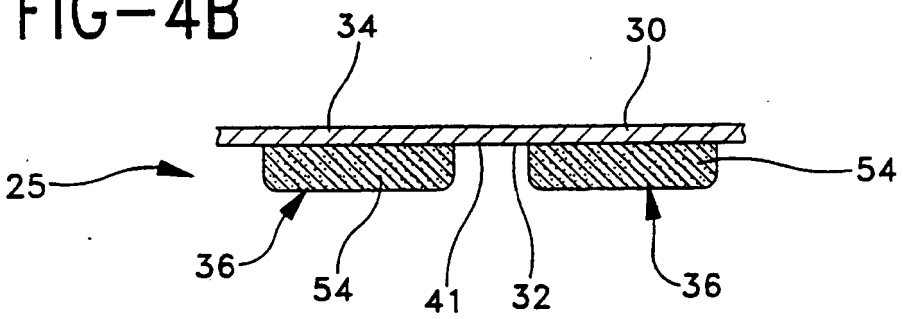


FIG-4C

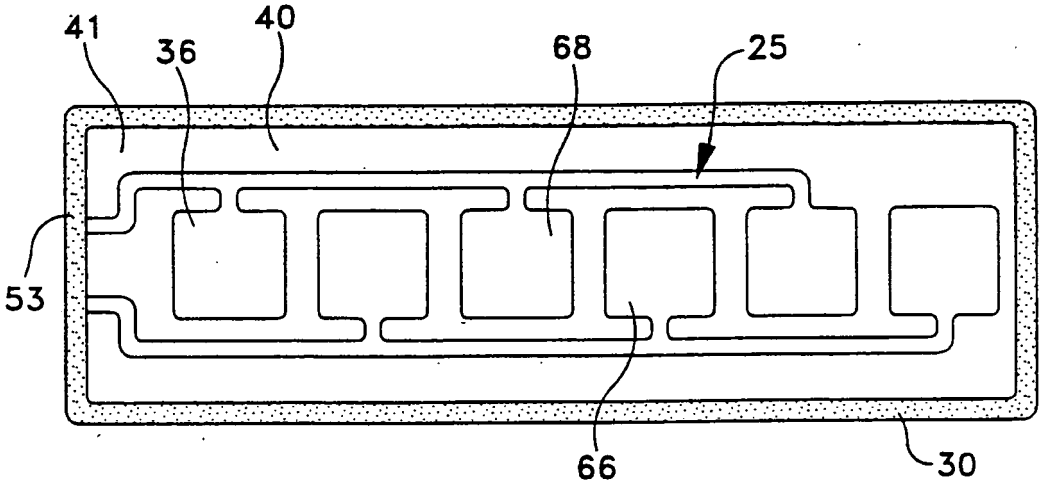
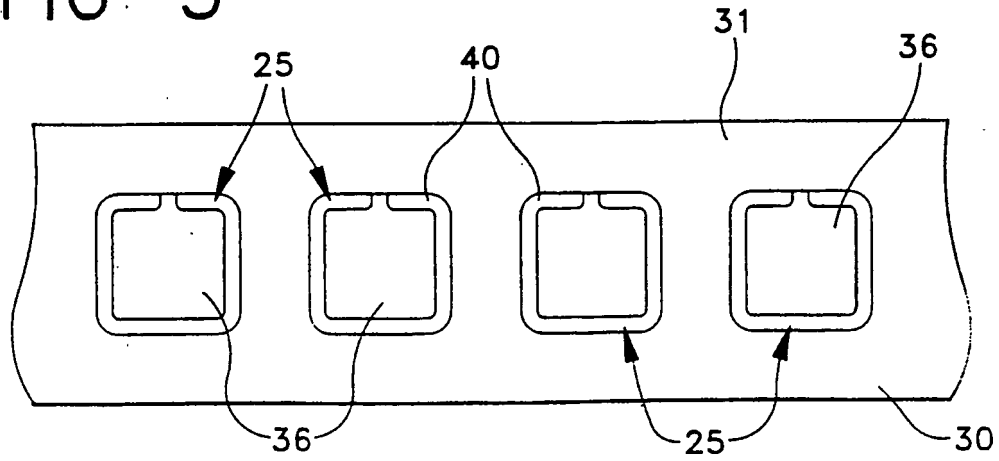


FIG-5



INTERNATIONAL SEARCH REPORT

In. .ational application No.
PCT/US94/01152

A. CLASSIFICATION OF SUBJECT MATTER
IPC(5) :A61N 1/30
US CL :604/20
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/20; 607/149-152

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

None

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US, A, 4,744,787, (Phipps et al.), 17 May 1988. See entire document.	1, 7, 20, 21, 27, 28 ---------- 2-6, 8-19, 22-26, 29-31
Y	US, A, 4,635,641, (Hoffmann), 13 January 1987. See Abstract, figures, and column 5 lines 44-47.	2-6, 8-11, 22-26, 31
Y	US, A, 4,883,457, (Sibalis), 28 November 1989. See column 4 lines 43-50, column 7 line 35 to column 8 line 57.	2-6, 8-19, 22-26, 31
Y	US, A, 5,254,081, (Maurer et al.), 19 October 1993. See Abstract.	29, 30

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
31 MARCH 1994	APR 20 1994
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE	Authorized officer MICHAEL RAFA Telephone No. (703) 308-2214

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INTERNATIONAL SEARCH REPORT

Int ational application No.
PCT/US94/01152

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 4,752,285, (Petelenz et al.), 21 June 1988. See Abstract.	1-31
A	US, A, 4,820,263, (Spevak et al.), 11 April 1989. See Abstract.	1-31
A	US, A, 5,053,001, (Reller et al.), 01 October 1991. See Abstract and figures.	1-31